Docket No.: IBIS-0007
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Inventor(s): Ecker et al.
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3/59 **Target** Accession Accession **Numbers** Number from Blast results Fetch Genbank Record Fetch Genbank Record for each Target Accession **Nucleotide** Number Sequence Genbank **BLAST** (Local) Record Similarity Search Blast Parse Results-Genbank Flat-file (not Records parsed) Parse Blast Results Annotations-Relational Database Blast Results-Relational DB

Figure 3

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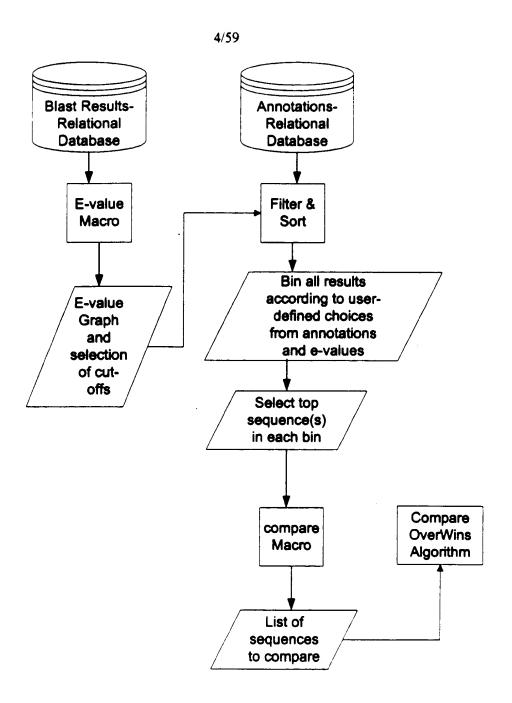


FIGURE 4

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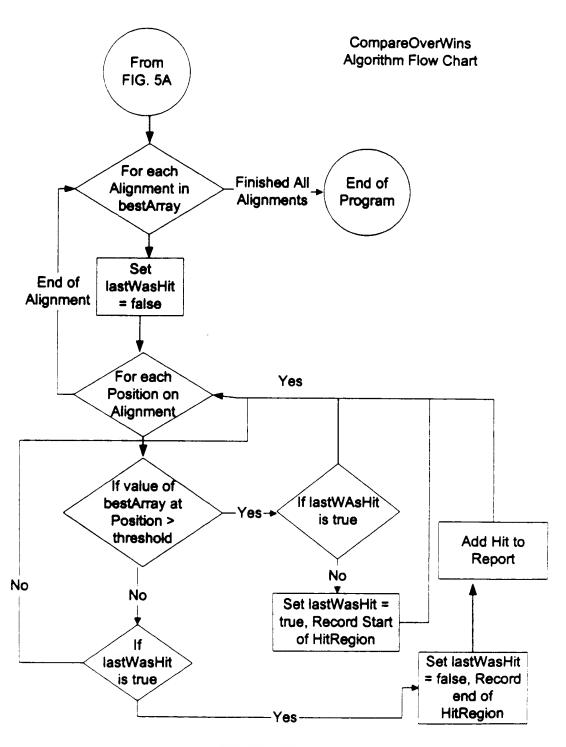


FIGURE 5B

.: IBIS-0007 DULATION OF MOLECULAR INTERACTION N RNA AND OTHER BIOMOLECULES Title: SITES Inventor(s): Ecker et al. Attorney: Paul K. Legaard Sheet 7 of 59

215-568-3100

Input: Sequence A length a Sequence B length b Window Size

7/59 CompareOverWins Algorithm Flow Chart **Basic Compare**

Output:

Array of size a by b of unsigned chars (0-255) Each point represents the number of matches in the window at that allignment and position

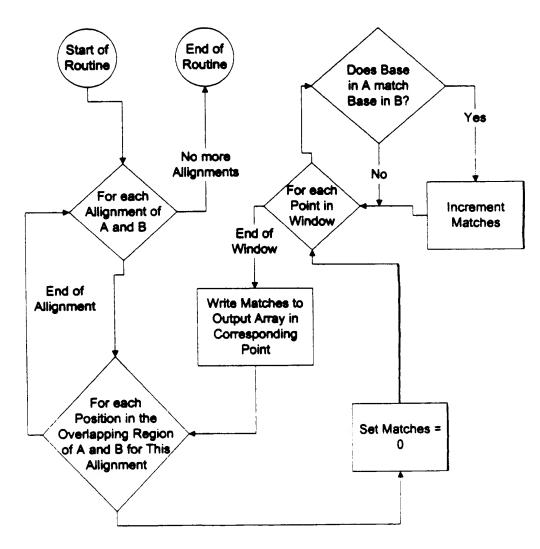
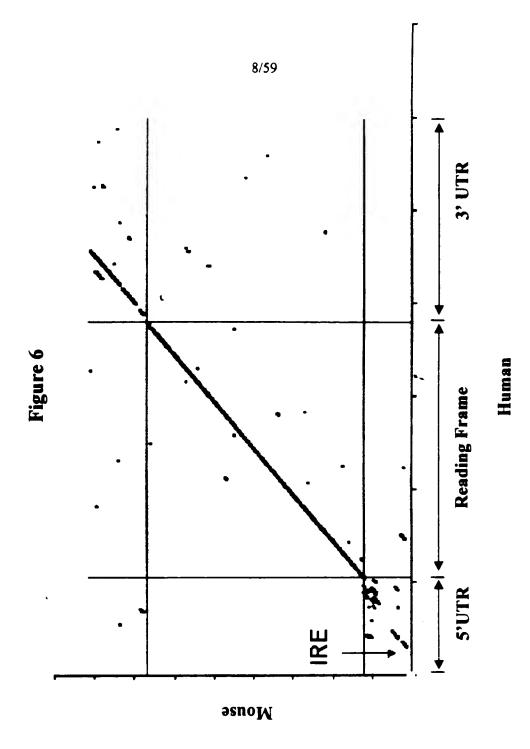


FIGURE 5C



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MUUMPUP

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CCCAP

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Self Complementation Analysis - Single Sequence

Figure 7

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Self Complementarity Comparisons 13 ortholog overlay 15.0 Complement 15.0 Complement 16.0 Complement 16.0 Complement 17.0 Complement 18.0 Comparisons 19.0 Complement 19.0 Comparisons 19.0 Comparisons

Ferritin IRE Region

Number of Orthologs

10/59

11/59

IRE String descriptor

HI

S2 H2

H2

S1

HI

for This descriptor allows of wobble (W)

· N can be any nucleotide · no mismatches.

to the stem · H refers region

· S refers to the single stranded region.

Stem-loop Model IX X

Z ZZZ ZZ Z ZZZZZ ZZZ J C

H2

5:5 NNNNN:NNNNN

6 CAGNGN

M2

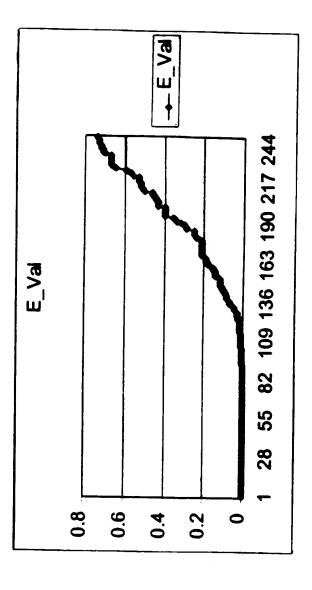
3:3 NNN:NNN

HI **S**1

Figure 9

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Sigure 10

Rocket No.: IBIS-0007 tle: MODULATION OF MOLECULAR INTERACTION SITES ON RNA AND OTHER BIOMOLECULES Inventor(s): Ecker et al. Attorney: Paul K. Legaard 215-568-3100 Sheet 45 of 59

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16S A Site rRNA

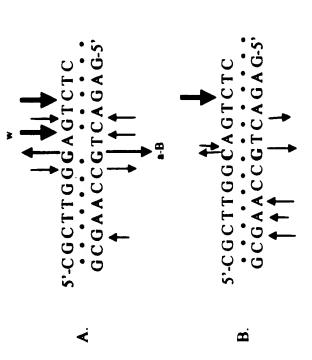
Control RNA

Figure 40

5'- GGCGUCA CACC U
CCGCUGA GUGG C
A
G
S'- GGCGUCACACC U
S'- GGCGUCACACC U
A
A
G
A
G

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SITS ON RNA AND OTHER BIOMOLECULES
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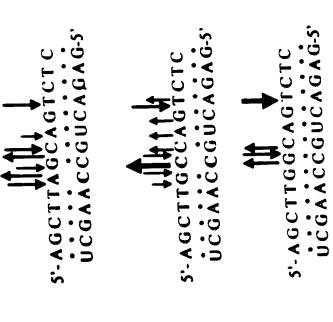
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igure 47

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Title: ULATION OF MOLECULAR INTERACTION SITE RNA AND OTHER BIOMOLECULES
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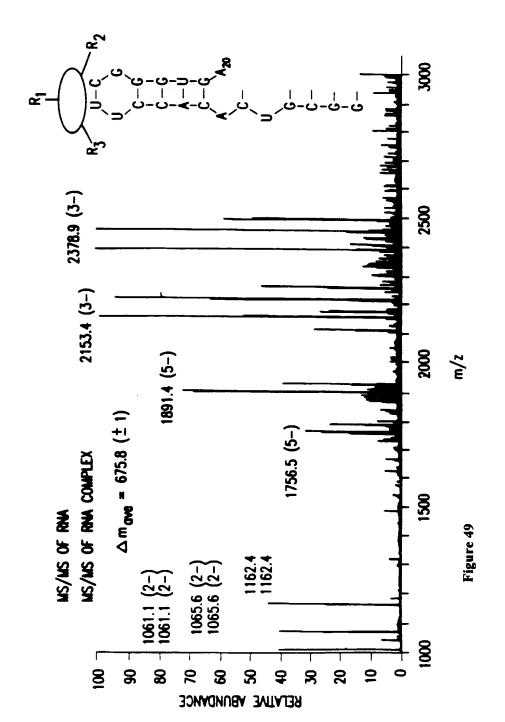
55/59



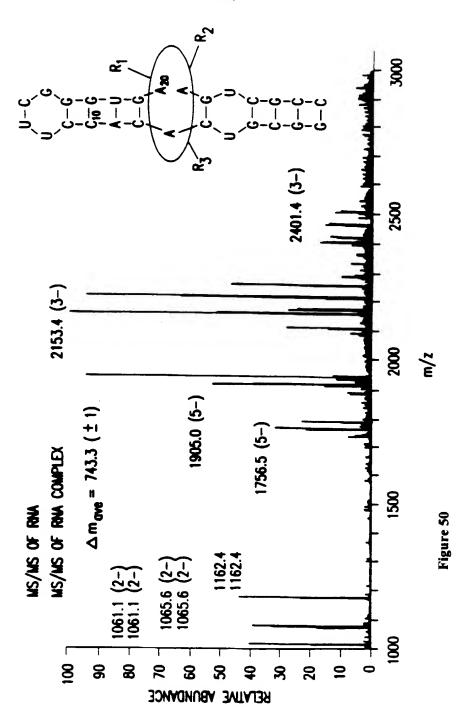
MS Fragmentation of DNA:RNA duplexes

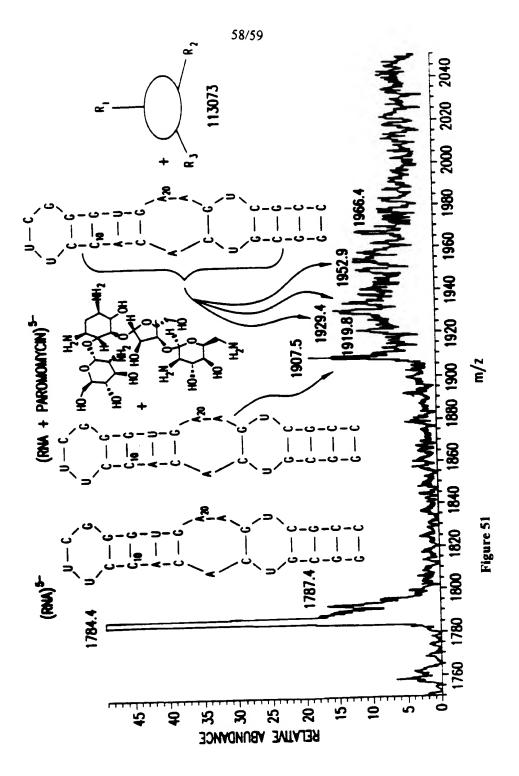
Figure 48











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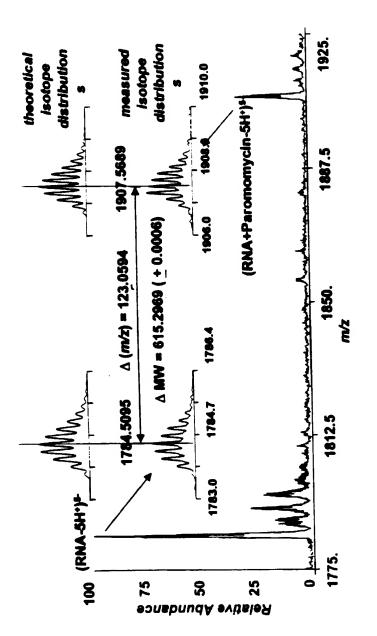


Figure 52

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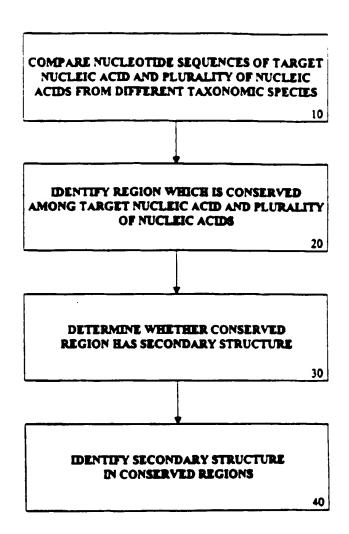
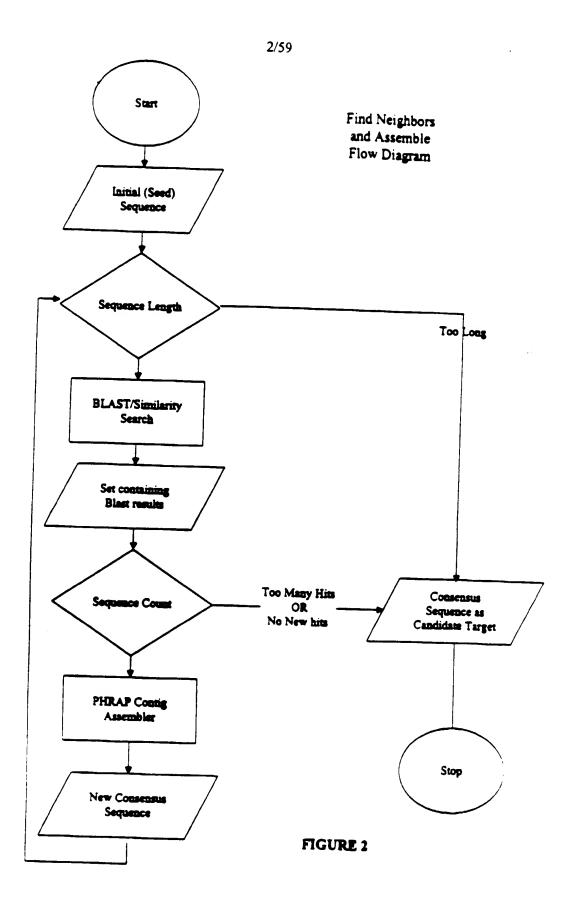


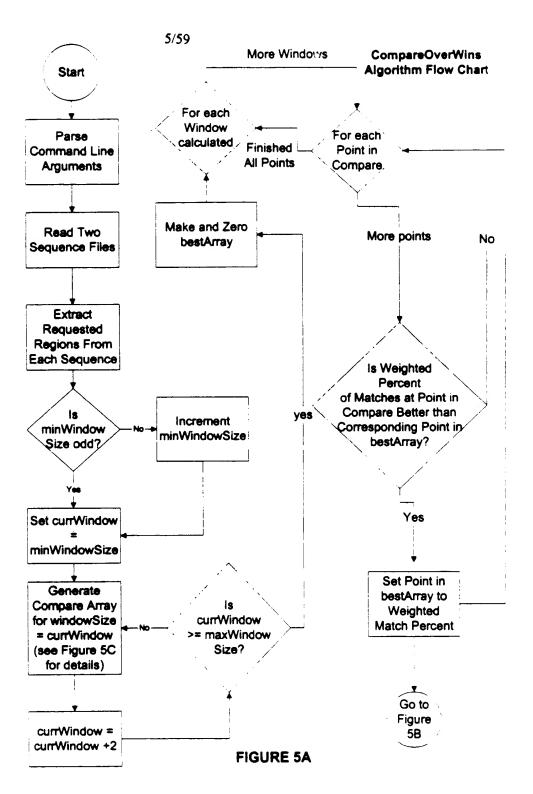
FIGURE 1

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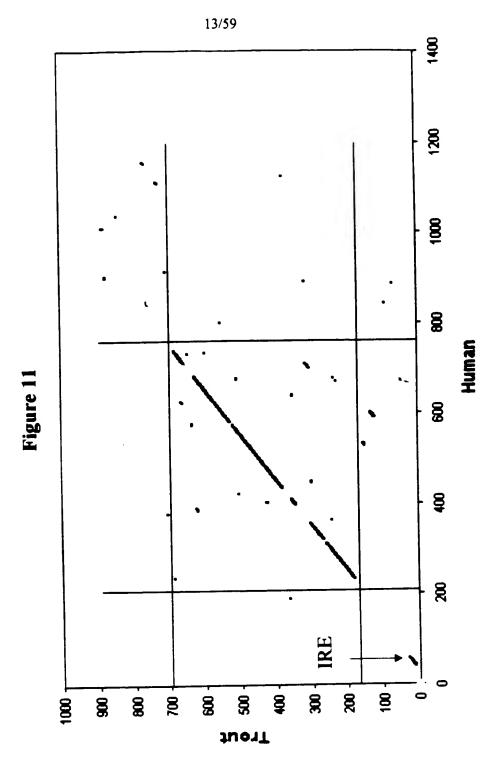


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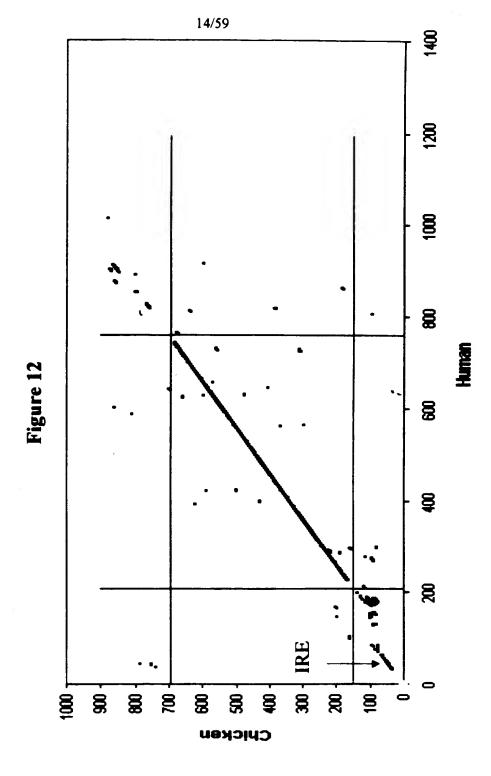
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Figure 13

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Compound CI

C12H18N2O5S

Fi

Fii

Fiii

Molecular formula

H₂NO

C₂H₄NO

C7H7O3S

Figure 14



Addition of fragments to yield compounds

	Table										
Fragment Identifier	Structure H	Name	Molecular formula	Other							
Fi	H-O-N-	Hydroxylamine	H ₂ NO	•••							
F _{ii}	CH ₃ CH ₃	Amino acid	C ₅ H ₄ NO								
F _{iii}	—————осн ₃	Sulfonyl	C ₇ H ₂ O ₃ S								

Figure 15

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Reagents	Identifier	Name	Properties
H-0-NH ₂ or P-0-NH ₂	Rį	Hydroxylamine	
CH ₃ CH ₃ HO N-FMOC	R _{ii}	FMOC blocked amino acid	. <u></u>
C1 OCH	, R _{iii}	Sulfonylchloride	

P = Solid support

Figure 16

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Transformation

Figure 17

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Common Fragment / Different Reagents and Transformations

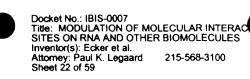
Figure 18

Dockston Io.: IBIS-0007
Title DULATION OF MOLECULAR INTERACTION
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Common Fragment / Different Reagents and Transformations

Figure 19A



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Common Reagent

Figure 19B

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Symbolic addition of fragments to yield compound

Symbolic Structure	Symbolic Identifier	Molecular formula
Fragment		
<u></u>	F _{i'}	CuHvNw
<u></u> -х	F _{ii'}	CuHyNw
x-OY	F _{iii'}	CuHvNw
Compound		
Z-00	Cľ	CuHvNw
		Moleculæ formula Fi
•		Molecular formula Fii'
		Molecular formula Fiji'
		- Molecular formula CI'

Figure 20

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Symbolic Reagent Table

Identifier	Name	Structure	Molecular formula
Rl	xxx	∠ CI	xxx
R2	. ·	CN0	•••
R3	•••	CI	
R4		Be	***
R5		G G	
R6	•••	Pg-O-OEt	
R7	•••	Pg—Cı	•••
R8	•••	Pg Br	•••
R9		PSI N3——PSI PSI	
R10		N ₃ Pgg	

Figure 21



Symbolic Fragment Table

<u>Identifier</u>	Symbolic Structure	Molecular formula	Molecular Weight
Fl	<u></u>	xxx	xxx
F2	<u></u> х	•••	
F3	○ -×		•••
F4	x x		
F5	x		
F6	x ✓ Y		
F7	xz		
F8	x z		

Figure 22

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Symbolic Transformation Table

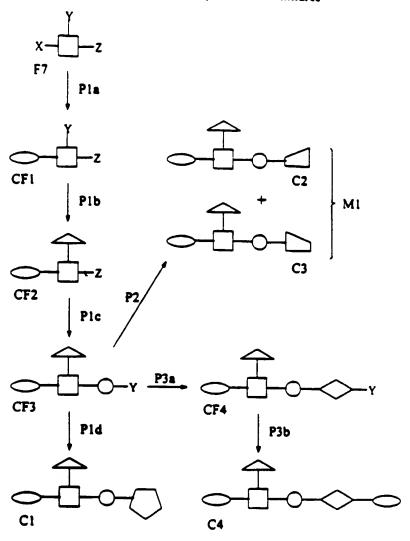
<u>Identifier</u>		Symbolic Reactions	Reagent
Tl	Fl	✓ X ← RI	conditions a
T2	F2	<u></u>	conditions B
Т3	F3	R3	conditions a
T4	F3		conditions a
Т5	F4		conditions a
T6	F5	x○	conditions &
T7	F5	x-○y ← R7	conditions a
T8	F6	X	conditions a
T9	F7	x—z R9	conditions y
TIO	F8	X RIC) conditions y

Figure 23

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Single Compounds and Mixtures



P = synthetic path F = fragment CF = complex fragment

M = mixture

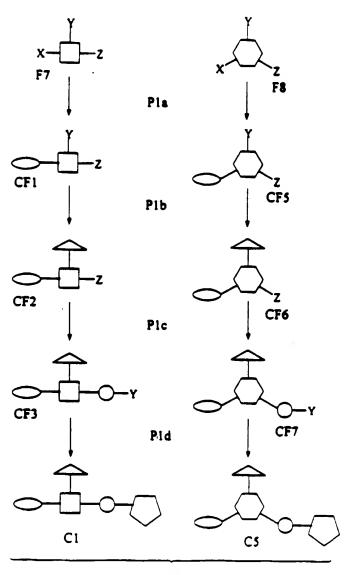
C = compound

Figure 24

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Mixture 2



M2

Figure 25

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Mixture 3

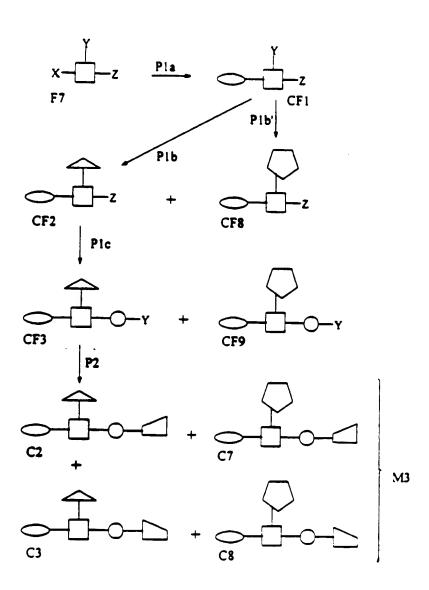
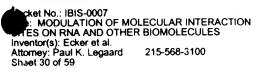


Figure 26



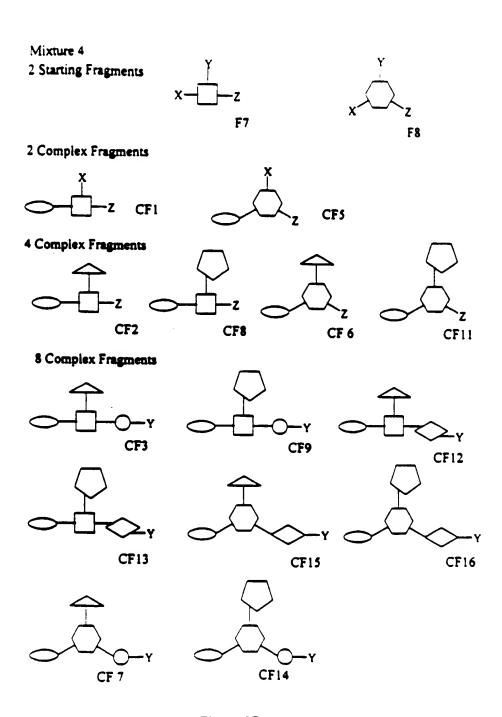


Figure 27A

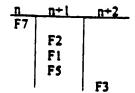
Mixture 4 (continued)

16 compounds

Figure 27B

Tracking Table for Compound C1

(a) By Fragments:



(b) By Transformations:

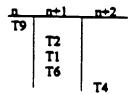


n n+1 n+2
T9 T2 T1
T6 T3

Synthesis Path 2

_	n+1	n+2
19		
	T2	
	Tl	
ı	17	
- 1		T3

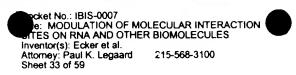
Synthesis Path 3



Synthesis Path 4

n	n+1	n+2
T9	_	
	T2	
	Tl	
	T7	
- (!	T4

Figure 28



Tracking Table

Tracking M1

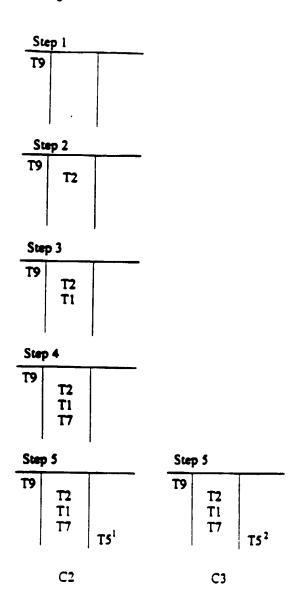


Figure 29

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Tracking Table

Tracking M2

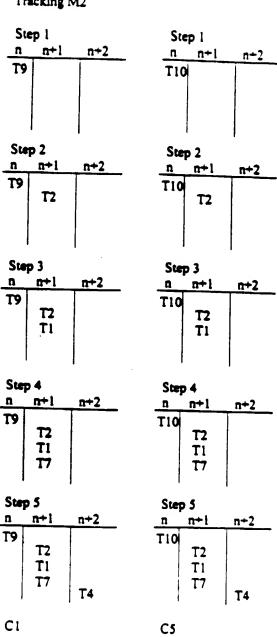


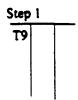
Figure 30

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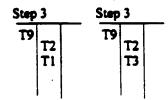
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Tracking Table

Tracking M3





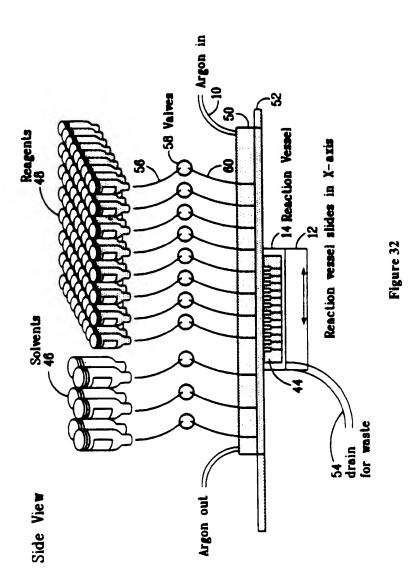


Step 4		Step	Step 4		
79	777	79	111		

Step	5	Step 5	St	ep 5	Step	5	
19	T2 T1 T7	T9 T2 T1 T7	T5 ²	79 173 177	T9	T2 T3 T7	T5 ²
	C2	C3		C7		C8	

Figure 31

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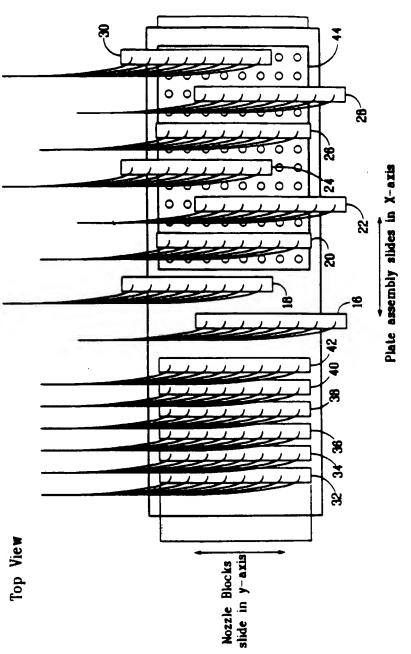


Figure 33

Synthesis of hydroxamic acids from alcohol resin

Figure 34

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litle: MODULATION OF MOLECULAR INTERACTION
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Synthesis of hydroxamic acids from hydroxylamine resin

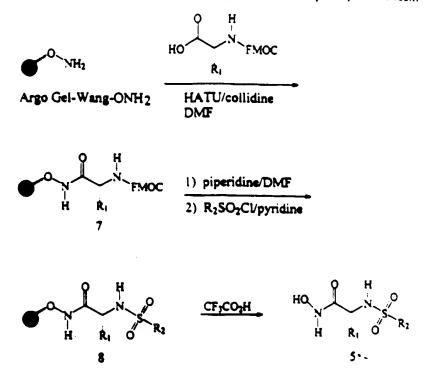
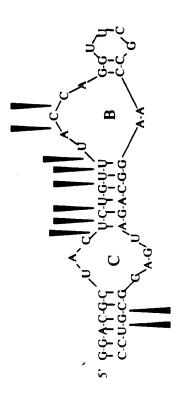
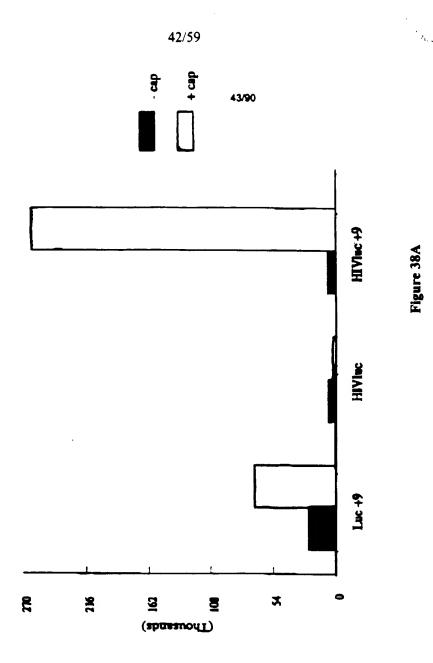


Figure 35

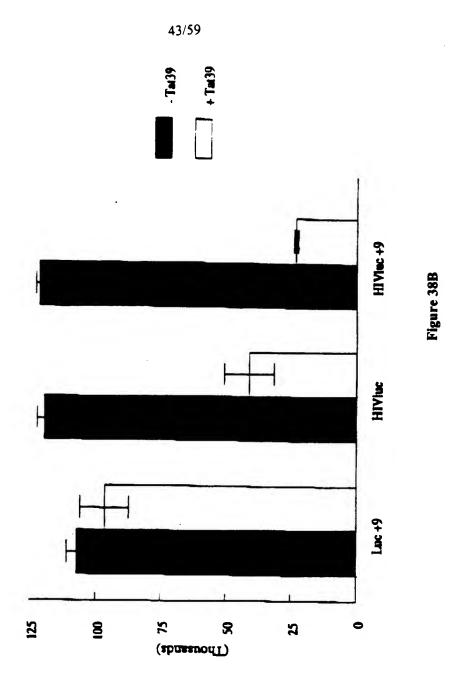
ocket No.: IBIS-0007
Itle: MODULATION OF MOLECULAR INTERACTION
SITES ON RNA AND OTHER BIOMOLECULES
Inventor(s): Ecker et al.
Attomey: Paul K. Legaard 215-568-3100
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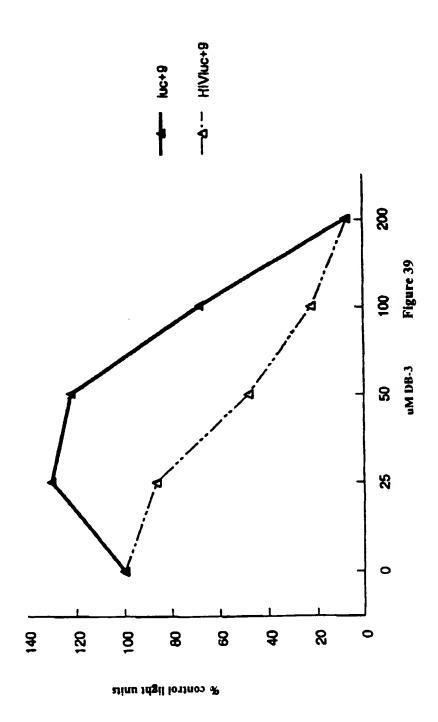
ာ အ	(M ¹)	% V	8	< 50
Calc. ∆G of binding	(kcal/mole)	-5.	-8.5	. .
Structure	O			
ACD Code		00001199	00192509	00003934



Pocket No.: IBIS-0007
Itle: MODULATION OF MOLECULAR INTERACTION
SITES ON RNA AND OTHER BIOMOLECULES
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Title: MODULATION OF MOLECULAR INTERACTIO
SITES ON RNA AND OTHER BIOMOLECULES
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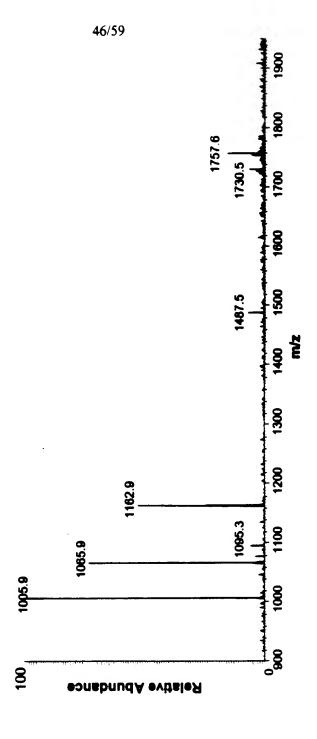
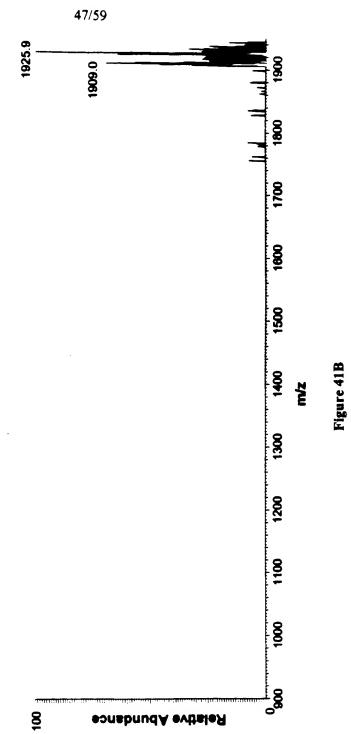


Figure 41A

Bocket No.: IBIS-0007
B: MODULATION OF MOLECULAR INTERACTION
ES ON RNA AND OTHER BIOMOLECULES
Inventor(s): Ecker et al.
Attorney: Paul K. Legaard 215-568-3100
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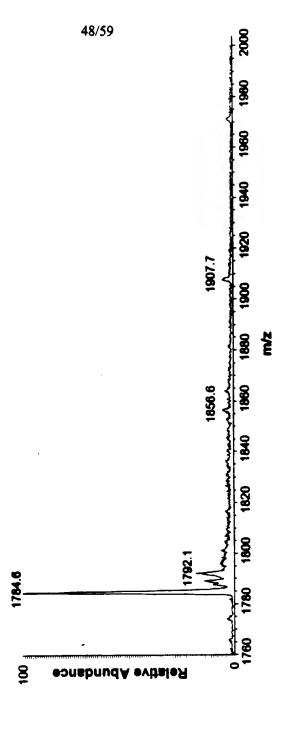


Figure 42A

Docket No.: IBIS-0007
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA AND OTHER BIOMOLECULES Inventor(s): Ecker et al.
Attorney: Paul K. Legaard 215-568-3100
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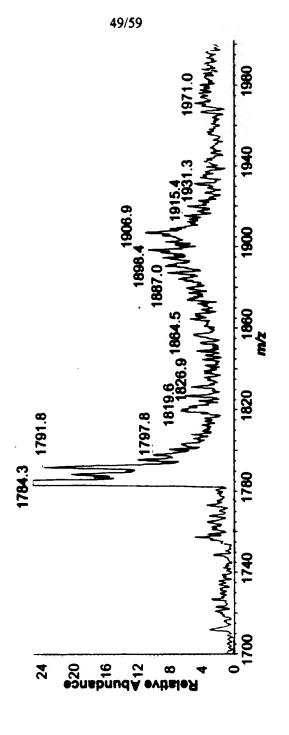
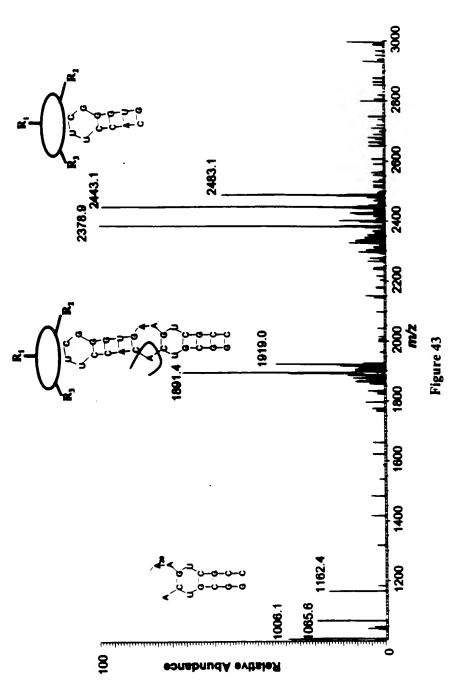
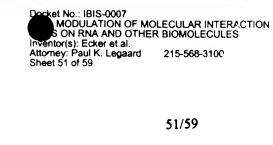
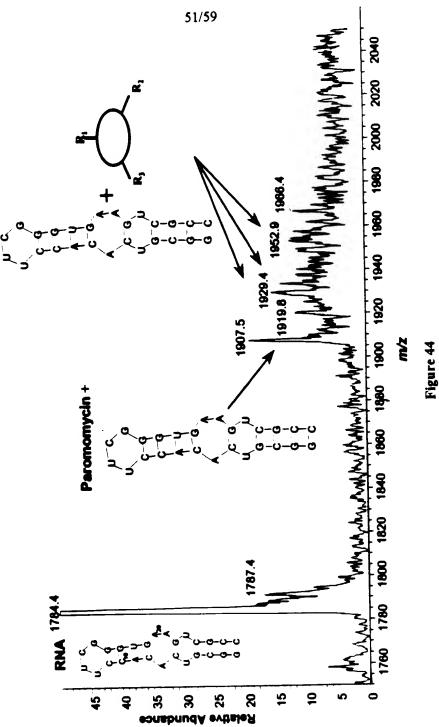


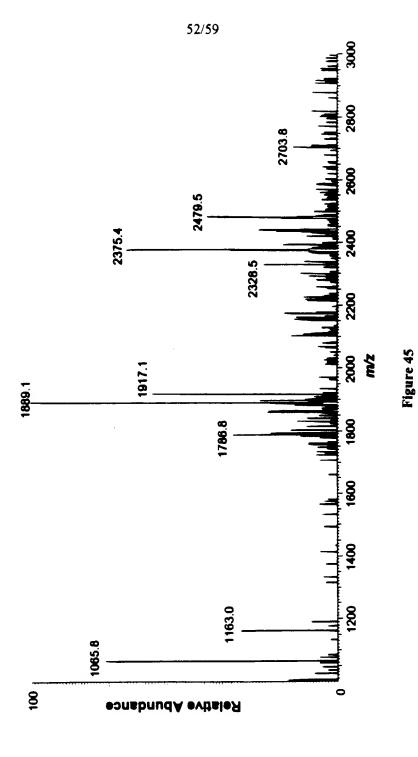
Figure 42B











Doctor No.: IBIS-0007
Title DDULATION OF MOLECULAR INTERACTION
SITS N RNA AND OTHER BIOMOLECULES
Inventor(s): Ecker et al.
Atto:ney: Paul K. Legaard 215-568-3100
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